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(54) Title: METHODS FOR OPTIMIZATION OF GENE THERAPY BY RECURSIVE SEQUENCE SHUFFLING AND SELECTION

(57) Abstract

The invention provides methods of evolving nucleic acids for use in gene therapy by recursive sequence recombination. Many of the methods evolve vectors, both viral and nonviral, to have improved properties. For example, vectors are evolved to have improved properties of viral titer, infectivity, expression of a gene within a vector, tissue specificity, viral genome capacity, episomal retention, lack of immunogenicity of the vectors or an expression product thereof, site-specific integration, increased stability, or capacity to confer cellular resistance to microorganism infection. The invention further provides an isolated O^6–methylguanine–DNA methyltransferase (MGMT) enzyme.